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European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR,
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(BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG).

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: USE OF COX-2 INHIBITORS FOR THE TREATMENT OF SCHIZOPHRENIA, DELUSIONAL DISORDERS, AFFECTIVE DISORDERS, AUTISM OR TIC DISORDERS

(57) Abstract: The invention concerns the use of a COX-2 inhibitor for the treatment of psychiatric disorders such as schizophrenia, delusional disorders, affective disorders, autism or tic disorders, in particular chronic schizophrenic psychoses and schizoaffective psychoses, temporary acute psychotic disorders, depressive episodes, recurring depressive episodes, manic episodes and bipolar affective disorders. Moreover, the invention is concerned with the use of a COX-2 inhibitor, in particular celecoxib, in combination with a neuroleptic drug, in particular risperidone, or an antidepressant, for the treatment of psychiatric disorders such as schizophrenia, delusional disorders, affective disorders, autism or tic disorders.



WO 02/102297 A3

INTERNATIONAL SEARCH REPORT

national Application No

PCT/EP 02/06013

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/635 A61K31/365 A61K31/54 A61K31/435 A61K31/42
A61P25/18 A61P25/24

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, EMBASE, MEDLINE, SCISEARCH, BIOSIS, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	EP 1 142 889 A (PFIZER PROD INC) 10 October 2001 (2001-10-10) paragraphs '0001!-'0005! paragraph '0082! claim 11	1-7
P,X	--- O'CONNOR J J ET AL: "NS-398, the cyclooxygenase-2 inhibitor attenuates long term depression in the rat dentate gyrus in vitro." SOCIETY FOR NEUROSCIENCE ABSTRACTS, vol. 27, no. 1, 2001, page 1025 XP001109452 31st Annual Meeting of the Society for Neuroscience; San Diego, California, USA; November 10-15, 2001 ISSN: 0190-5295 the whole document ---	1-7



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

Z document member of the same patent family

Date of the actual completion of the international search

15 January 2003

Date of mailing of the international search report

21/01/2003

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 02/06013

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 25353 A (HILL RAYMOND GEORGE ;MERCK SHARP & DOHME (GB); WHITING PAUL JOHN ()) 27 May 1999 (1999-05-27) page 1 page 37, paragraph 2 claims 15,19-21	8-12,20
A	LANTZ M S (REPRINT) ET AL: "Acute onset of auditory hallucinations after initiation of celecoxib therapy" AMERICAN JOURNAL OF PSYCHIATRY, (JUN 2000) VOL. 157, NO. 6, PP. 1022-1023 PUBLISHER: AMER PSYCHIATRIC PRESS, INC, 1400 K ST, N W, STE 1101, WASHINGTON, DC 20005. ISSN: 0002-953X., XP001133838 the whole document	
X	JIANG H-K ET AL: "NON-STEROIDAL ANTI-INFLAMMATORY DRUGS WITH ADVERSE PSYCHIATRIC REACTIONS: FIVE CASE REPORTS" CLINICAL RHEUMATOLOGY, ACTA MEDICA BELGICA, BRUXELLES, BE, vol. 18, no. 4, 1999, pages 339-345, XP001007036 ISSN: 0770-3198 the whole document	20,22,23
A	SRAMEK, JOHN J. ET AL: "The status of ongoing trials for mild cognitive impairment" EXPERT OPINION ON INVESTIGATIONAL DRUGS (2001), 10(4), 741-752 , XP008012341 page 748, column 2, paragraph 1	1-7

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 02/06013.

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 1-19 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1-3,7-15,18-23 relate to a compound defined by reference to a desirable characteristic or property, namely the activity as COX2 inhibitor, neuroleptic, antidepressant.

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds.

In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to its pharmacological profile.

Present claims 4,7,11,18,19,23 relate to an extremely large number of possible compounds (chromen derivative, chroman derivative; prodrugs thereof). Support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed.

Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds mentioned in claim 4, and the compounds mentioned in the description in Formulas I, II and III, alone or together with the compounds mentioned in claim 13,14,16,17,24,25.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 02/06013

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 1142889	A	10-10-2001	CA 2343459 A1	03-10-2001
			EP 1142889 A1	10-10-2001
			JP 2001316387 A	13-11-2001
			US 2002115856 A1	22-08-2002
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WO 9925353	A	27-05-1999	AU 1041599 A	07-06-1999
			WO 9925353 A1	27-05-1999
			US 6174886 B1	16-01-2001
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			US 6110915 A	29-08-2000
			US 6063783 A	16-05-2000
			US 6107296 A	22-08-2000
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